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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,448	11/07/2001	David Lewis	Mirus.030.03	3784

25032 7590 08/22/2007

MIRUS CORPORATION
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MADISON, WI 53719

EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/007,448	LEWIS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-9, and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on August 10, 2007 has been entered.

Claim 1 has been amended.

Claims 1, 3-9, and 13-16 are pending in the instant application.

Claims 1, 3-9, and 13-16 have been examined on the merits.

Response to Arguments

Applicants Amendment and Response filed August 10, 2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed March 3, 2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Priority

It is noted that the instant application claims benefit for this application under 35 U.S.C. 120 as a continuation in part of USSN 09/447,966, now U.S. Patent No.

6,627,616, filed November 29, 1999; which claims benefit to provisional applications 60/121,730 and 60/146,564, filed February 26, 1999 and July 30, 1999, respectively; which is a continuation in part of nonprovisional application USSN 09/391,260, now abandoned, filed September 7, 1999; which is a divisional of nonprovisional application USSN 08/975,573, now U.S. Patent No. 6,265,387, filed November 21, 1997; which is a continuation of USSN 08/571,536, now abandoned, filed December 13, 1995.

The Examiner would like to point out that the instant application claims priority to a laundry list of U.S. Provisional Applications, U.S. Patent Applications, and Patented U.S. Applications. Due to the voluminous nature and number of the applications to which priority is claimed, Applicant are requested to point out with particularity where support for the instantly claimed invention may be found in one or more of the prior filed applications to which benefit is claimed, since such support is not readily apparent in the priority documents.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The Examiner fully acknowledges Applicant's claim for benefit, however, the instant claims have been afforded priority to USSN 09/447,966, now U.S. Patent No. 6,627,616, filed November 29, 1999 because support for the claims, drawn to a process

for delivering, without a transfection reagent used in the prior art, a polynucleotide into a cell of a mammal to inhibit, eliminate, or alter expression of an endogenous nucleotide sequence could not be found in any earlier application which Applicants claim priority to.

In sum, support for a process for delivering, without a transfection reagent used in the prior art, a polynucleotide into a cell of a mammal to inhibit, eliminate, or alter expression of an endogenous nucleotide sequence is only found in parent application USSN 09/447,966, but not in any other application which Applicants claim priority to. Therefore, the instant application and claims have been afforded priority November 29, 1999.

If Applicants believe that they are entitled to an earlier priority date, the Examiner urges Applicant to specifically point where support can be found for a process for delivering, without a transfection reagent used in the prior art, a polynucleotide into a cell of a mammal to inhibit, eliminate, or alter expression of an endogenous nucleotide sequence in any earlier application Applicants claim priority to.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-9, and 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term, "the naked polynucleotide" in parts (a), (b), and (d). There is insufficient antecedent basis for this term in the claim because the preamble of the claim never makes reference to a "naked polynucleotide". Appropriate correction is required. Claims 3-9 and 13-16 are included in this rejection because of their dependency therein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-6, 8 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumasaka et al. (Journal of Clinical Investigation, 1996 Vol. 97:2362-2369, made of record in the Office Action filed November 23, 2004).

Claim 1 is drawn to a process for delivering, without a transfection reagent used in the prior art, a polynucleotide into a cell of a mammal to inhibit, eliminate, or alter expression of an endogenous nucleotide sequence comprising making the polynucleotide consisting of a sequence that is complementary to a nucleic acid sequence in the mammal, inserting the polynucleotide into a vessel in the mammal,

wherein the vessel consists of arteries, arterioles, capillaries, venules, sinusoids, veins, lymphatics, and bile ducts, increasing the permeability of the vessel within the target tissue, and delivering the polynucleotide to the cell wherein the sequence expression is inhibited, eliminated, or altered. Claims 3-6, 8, and 13-15 are dependent on claim 1 and include all the limitations of claim 1, with the further limitations, wherein vessel permeability is increased by increasing pressure against vessel walls by increasing a volume of fluid within the vessel, wherein the vessel is a tail vein, wherein the cell is selected from a liver, spleen, heart, kidney, muscle or lung cells, and wherein the pressure increases extravascular volume.

Kumasaka et al. disclose a process for delivering a polynucleotide, ISIS 3082, without a transfection reagent into a cell of a mammal via intravenous injection. Kumasaka et al. disclose that ICAM-1 mRNA expression was detected and inhibited in the lung (see Figures 1 and 2). Kumasaka et al. disclose ISIS 3082 was injected into BALB/C mice through the tail vein and neutrophil emigration was detected in the lungs (see Figure 4).

It is noted that injection into the tail vein with ISIS 3082 is equivalent to increasing vessel permeability within the target tissue, by increasing pressure against vessel walls, increasing a volume of fluid within the vessel, and increasing extravascular volume as claimed because the method of intravascular injection would inherently increase pressure in the area of injection and at the point of injection. The pressure against the vessel walls would inherently be increased because the needle used is external to the tail vein.

Therefore Kumasaka et al. anticipate claims 1, 3-6, and 13-15.

Response to Arguments

It is noted that a similar rejection was made of record in the Office Action mailed July 27, 2005 and was maintained in the Office Action mailed March 9, 2007. In response to this rejection, Applicants argue that the claims have been amended to perfect priority to Patent No. 6,627,616, filed November 29, 1999. Applicants contend that this priority date should obviate the instant rejection.

This argument has been fully considered, but is not found persuasive because while Applicants have perfected their priority date to be November 29, 1999, the reference of Kumasaka et al. was published in 1996 and therefore constitutes as 102(b) art against the instant claimed invention.

Therefore Kumasaka et al. anticipate claims 1, 3-6, and 13-15.

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Claim 1, 3-6, 8, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Graham et al. (Journal of Pharmacology and Experimental Therapeutics, 1998 Vol. 286:447-458, made of record in the Office Action filed November 23, 2004).

Claims 1, 3, 4, 5, 6, 8, and 13-15 are described above in the rejection against claims 1, 3-6, and 13-15 as being anticipated by Kumasaka et al. Claim 16 is dependent on claim 1 and includes all the limitations of claim 1, with the further limitation wherein the vessel consists of liver.

Graham et al. disclose a process for delivering a polynucleotide, ISIS 1082, without a transfection reagent into a cell of a mammal via intravenous injection through the tail vein. Graham et al. disclose the metabolism, pharmacokinetics, and intraorgan distribution of the oligonucleotide in tissues such as the liver (see Figures 2-5, 11, and 12).

It is noted that injection into the tail vein with ISIS 1082 is equivalent to increasing vessel permeability within the target tissue, by increasing pressure against vessel walls, increasing a volume of fluid within the vessel, and increasing extravascular volume as claimed because the method of intravascular injection would inherently increase pressure in the area of injection and at the point of injection. The pressure against the vessel walls would inherently be increased because the needle used is external to the tail vein. It is further noted that Graham et al. are silent regarding the effect of ISIS 1082 on inhibiting or eliminating expression of an endogenous nucleotide sequence. However, given the quantitative pharmacokinetic information provided by Graham et al. following intravenous administration of ISIS 1082, one of skill in the art would conclude that inhibition of gene expression would result to some degree, absent evidence to the contrary.

Therefore Graham et al. anticipate claims 1, 3-6, 8, and 13-16.

Response to Arguments

It is noted that a similar rejection was made of record in the Office Action mailed July 27, 2005 and was maintained in the Office Action mailed March 9, 2007. In

response to this rejection, Applicants argue that the claims have been amended to perfect priority to Patent No. 6,627,616, filed November 29, 1999. Applicants contend that this priority date should obviate the instant rejection.

This argument has been fully considered, but is not found persuasive because while Applicants have perfected their priority date to be November 29, 1999, the reference of Graham et al. was published on July, 1998, which is more than a year before Applicant's priority date. Therefore, Graham et al. constitutes as 102(b) art against the instant claims.

Therefore Graham et al. anticipate claims 1, 3-6, 8, and 13-16.

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Claims 1, 3, 4, 5, 7, 9, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Kay et al. [U.S. Patent No. 6,107,027, made of record in the Office Action filed November 23, 2004].

Claims 1, 3, 4, 5, 9, and 13-15 are described above in the rejection against claims 1, 3-6, and 13-15 as being anticipated by Kumasaka et al. Claim 7 is dependent on claim 1 and includes all the limitations of claim 1 and provides the further limitation, wherein the vessel consists of a bile duct.

Kay et al. disclose a method for inhibiting hepatitis C virus (HCV) gene expression in cells comprising administering, without the aid of a transfection reagent, an adenovirus encoding a HCV ribozyme, which inhibits the hepatitis C virus (see claim 1). Kay et al. further disclose the adenovirus encoding a HCV ribozyme, which inhibits

the hepatitis C virus RNA, is infused via the bile duct (see claim 7), inhibits hepatocyte cells (see claim 2), and inhibits hepatic mRNA expression in transgenic mice (see Figure 4B).

It is noted that injection into the bile duct with the adenovirus encoding a HCV ribozyme is equivalent to increasing vessel permeability within the target tissue, by increasing pressure against vessel walls, increasing a volume of fluid within the vessel, and increasing extravascular volume as claimed because the method of injection would inherently increase pressure in the area of injection and at the point of injection. The pressure against the vessel walls would inherently be increased because the needle used is external to the bile duct.

Therefore, Kay et al. anticipate claims 1, 3, 4, 5, 7, 9, and 13-15.

Response to Arguments

It is noted that a similar rejection was made of record in the Office Action mailed July 27, 2005 and was maintained in the Office Action mailed March 9, 2007. In response to this rejection, Applicants argue that the claims have been amended to perfect priority to Patent No. 6,627,616, filed November 29, 1999. Applicants contend that this priority date should obviate the instant rejection.

This argument has been fully considered, but is not found persuasive because while Applicants have perfected their priority date to be November 29, 1999, the reference of Kay et al. was issued on August 22, 2000, but was filed September 11,

2005. Given this information, Kay et al. constitutes as 102(e) art against the instant claims.

Therefore, Kay et al. anticipate claims 1, 3, 4, 5, 7, 9, and 13-15.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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tcg
August 18, 2007
/Terra Cotta Gibbs/